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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/018,604	06/25/2002	Tove Martel Ida Else Christensen	DYOU27.001APC	8385

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EXAMINER	
SAIDHA, TEKCHAND	
ART UNIT	**PAPER NUMBER**
1652	

DATE MAILED: 04/26/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/018,604	CHRISTENSEN ET AL.	
	Examiner	Art Unit	
	Tekchand Saidha	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 February 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6,8-10,14-18,20,21 and 37-50* is/are pending in the application.

4a) Of the above claim(s) *37,39-41 and 43-50* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6,8-10,14-18,20,21,38 and 42* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *14 December 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Final Rejection

1. Applicants' amendment filed February 18, 2005, in response to Office Action mailed August 31, 2004, is acknowledged.

2. Claims 1-6, 8-10, 14-18, 20-21 & new claims 37-50 are present in this application.

3. Applicants' previously elected **Group I**, claim(s) 1-23, drawn to a process of modifying pectin by silencing polygalacturonase (PG) activity in a host cell having Pectin methylesterase (PME) [E.C. 3.1.1.11] and PG activities.

4. **Claims withdrawn** :

New claims 37, 39-41 & 43-50 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention, wherein the added new claims recite distinct method steps and do not require the DNA sequence in the antisense orientation.

5. Claims 1-6, 8-10, 14-18, 20-21, 38 & 42 are pending and under consideration in this examination.

6. Applicant's arguments filed as per the amendment cited above have been fully considered but they are not deemed to be persuasive. The reasons are discussed following the rejection(s).

7. Any objection or rejection of record which is not expressly repeated in this Office Action has been overcome by Applicant's response and withdrawn.

8. Enclosed here are a signed copy of PTO-1449 submitted 2/18/2005, as well as PTO-892, citing EP 0532060 A1 and Grierson et al (1986, Nucleic Acid Reviews, 14 p 8595-2603), along with a copy each of the references cited, which were inadvertently missed out from the Office Action mailed August 31, 2004.

9. Applicants request citing all the detailed information considered by the Examiner by including the references in form PTO-892 based upon search information retrieved from IFW.

Only references cited in the Office Action considered relevant are included in form PTO-892, and not the entire search.

10. The information disclosure statement filed 2/18/2005 fails to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each cited foreign patent document; each non-patent literature publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed. It has been placed in the application file, but the information referred to therein has not been considered. No copies of foreign patent document or non-patent literature publication have been received.

11. ***35 U.S.C. 112, first paragraph (Written Description)***

Claims 1-6, 8-10, 14-18, 20-21, 38 & 42 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

Claim 1-6, 8-10, 14-18, 20-21, 38 & 42 are directed to a process of modifying pectin by (i) providing a host having native pectin methyl esterase (PME) and polygalacturonase (PG) activity; (ii) transforming said host by silencing PG activity, thereby providing increased PME to PG ratio; (iii) preparing a PME extract from the transformed host; (iv) treating the pectin with PME extract to modify the pectin, the claimed genus.

The specification, however, only provides a single representative species of a process of modifying pectin by (i) providing a tomato plant host having native pectin methyl esterase (PME) and polygalacturonase (PG) activity; (ii) transforming said host by silencing PG activity, wherein the PG activity is silenced by expression of a nucleic acid sequence of SEQ ID Nos. 1 or 3 in an antisense orientation, thereby providing increased PME to PG ratio; (iii) isolating or preparing a PME extract from the transformed plant; (iv) treating the pectin with PME extract, and (v) isolating the de-esterified pectin. No

variants, homologs, fragments thereof or parts of a nucleotide sequence in the antisense orientation are described.

The specification also fails to describe additional representative species of these processes whereby any host can be transformed with in PG encoding nucleic acid in an anti-sense orientation by any identifying structural characteristics other than the properties or activity recited in claims, for which no predictability of structure is apparent. Given this lack of additional representative species, Applicants have failed to sufficiently describe the claimed invention, in such full, clear, concise, and exact terms that a skilled artisan would recognize Applicants were in possession of the claimed invention.

12. ***Enablement***

Claims 1-6, 8-10, 14-18, 20-21, 38 & 42 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a process of modifying pectin by (i) providing a tomato plant host having native pectin methyl esterase (PME) and polygalacturonase (PG) activity; (ii) transforming said host by silencing PG activity, wherein the PG activity is silenced by expression of a nucleic acid sequence of SEQ ID Nos. 1 or 3 in an antisense orientation, thereby providing increased PME to PG ratio; (iii) isolating or preparing a PME extract from the transformed plant; (iv) treating the pectin with PME extract, and (v) isolating the de-esterified pectin, does not reasonably provide enablement for all any host wherein the native PME & PG activities are silenced by expression of any PG encoding nucleic acid in the antisense orientation. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. Factors to be considered in determining whether undue experimentation is required have been described above. The factors most relevant to this rejection are the scope of the claims, unpredictability in the art, the amount of direction or guidance presented, and the amount of experimentation necessary.

The claim is drawn to encompass any host, which may be a cell, tissue, organ or plant and transforming host by silencing PG activity or expression of nucleic acid sequences, or parts (fragments) thereof, homologue or variants thereof in an antisense orientation, from any source. While the specification discloses possible tomato plant as the host and SEQ ID Nos. 1 and 3 as the PG silencing nucleotides. Despite knowledge in the art for the production of numerous PG encoding nucleic acids which can be constructed in the antisense orientation in order to limit or abolish PG expression in the host, the specification fails to provide additional guidance regarding structure or construction of such antisense molecules from any source or structure of nucleic acid(s) parts (fragments), homologues or variants which can be effective in limiting or abolishing PG expression. Further, as is well known in the 'antisense technology', "antisense" refers to an expressed nucleotide sequence which is complementary to, and can therefore be effective in forming a duplex with the native nucleic acid or gene or a naturally expressed nucleotide sequence associated with the native PG enzyme [see for example, page 14 of the instant specification]. Based upon what is known in the prior art it would be highly unpredictable for one skilled in the art to silence the PG activity by expressing any portion of a PG encoding nucleotide or part or homolog or variant thereof of a nucleotide sequence of SEQ ID NO: 1 or 3, without specifically modifying at least a portion of the target gene product or PG, for example (see USP 6,271,033 cited in Applicants IDS filed 2/18/2005, claims 1-8, for example). Applicants' specification provide no guidance to the structure & size of the portions (or fragments) or homolog or variant thereof of a nucleotide sequence of SEQ ID NO: 1 or 3, that would be capable of functionally silencing or blocking PG activity at least in part.

While recombinant techniques are known, it is <u>not</u> routine in the art to screen large numbers of PG encoding nucleotides, or prepare host cells transformed with part(s) of a nucleotide sequence in an antisense orientation;

or prepare transformed host cells comprising variants, homologues or fragments of SEQ ID NO : 1 or 3, which may be effective in silencing PG activity; or a process wherein the activity of the native PG enzyme of SEQ ID NO: 2 or a variant, homologue or fragment thereof is silenced by expression of a part of a nucleotide sequence (ex. Claim 3); and which may be used in preparing a PME extract and which can be further modify pectin. Therefore, one skilled in the art would require guidance to the structures and/or size of various PG silencing molecules as well as occurrence or methods of preparation of homologues or variants in order to make and use the PME having silenced PG enzyme in the claimed process in a manner reasonably commensurate with the scope of the claim. Without such guidance, the experimentation left to those skilled in the art is undue.

Applicants' arguments:

Applicants address the written description and enablement rejections together (see Applicants response, pages 10-41).

Applicants argue based upon claims to U. S. Patent No. 6,271,033, granted by U. S. Patent Office, and hence determined to have been described and enabled by the disclosure. U. S. Patent No. 6,271,033, provide a method for modifying the production of a target gene product in a plant cell wherein the method comprises transforming the plant cell with a construct comprising a recombinant DNA sequence coding for only a part of the target gene product, wherein the target gene product is fruit ripening enzyme, wherein the fruit ripening enzyme is a polygalacturonase, pectinesterase, etc., wherein said DNA sequence being shorter than the sequence encoding polygalacturonase or pectinesterase, etc., but sufficient to inhibit the expression of the enzyme(s). Applicants further argue that U. S. Patent No. 6,271,033 is evidence, if not conclusive, that method of silencing PG in a host cell were well known to those of ordinary skill in the art at the time the present priority application was filed.

Applicants submit that the attached U. S. Patent No. 6,271,033, is also an acknowledgement by the Patent Office that specific host cells or sequences were not required to practice the claimed method. The subject matter of U. S. Patent No. 6,271,033 and 5,296,376, were extensively considered by the Patent Office Examiners and the Board of Appeals.

Applicants' arguments are considered but not found persuasive because the allowed claims in US patent 5,296,376, are to 'A construct having the structure of pJR16S (very specific), and claims to U. S. Patent No. 6,271,033, are to 'method of modifying the production of a target gene product – wherein the DNA sequence codes for at least a part of the target gene product, thus defining the fragment by functionality. The patented claims are narrower in scope than the instant claims and guidance to PG several fragments, antisense. sense molecules and vectors is provided in **Table 1** (of USP 6,271,033). Applicants' claims on the other hand provide no reference to the size of the portions (or fragments) or the nature of homolog(s) or variant(s) in relation to nucleotide sequence of SEQ ID NO: 1 or 3, that would be capable blocking PG activity (functionality) at least in part. The written description and enablement rejections are maintained mainly for this reason. Claim language reciting DNA sequences of SEQ ID Nos. 1 or 3, is suggested to overcome this rejection.

The teachings of Grierson et al. is cited in Applicants' specification on page 16, and specifically teaches a ripening related cDNA (pTOM6) encoding the predicted amino acid sequence of polygalacturonase (see Applicants' drawings, Figure 1). A copy of the reference is provided, but the reference is no longer cited in view of Applicants' arguments.

13. ***Claim Rejections - 35 USC §112*** (second paragraph)

Claims 1-6, 8-10, 14-18, 20-21, 38 & 42 are rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, 37, recite abbreviation 'PME' which the Applicants have designated as 'polymethylesterase'. The claims are indefinite because the first use of a 'not so common' abbreviation is incorrectly spelled out. PME stands for 'pectin methyl esterase'.

Claims 2-6, 8-10, 14-18, 20-21, 38 & 42 are included in this rejection for failing to correct the defect present in the base claim. Claim 37 is not under examination in this application, however, claims 38 & 42 are dependent upon the claim 37, hence the reference to claim 37.

14. Claims 38 & 42 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claims 38 & 42 depend from claim (new) 37, and are drawn to a non-elected invention, wherein the added new claims recite distinct method steps and do not require the DNA sequence in the antisense orientation. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form.

15. Having considered Applicants' arguments the obviousness rejection under 35 USC 103 is withdrawn.

16. No claim is allowed.

17. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

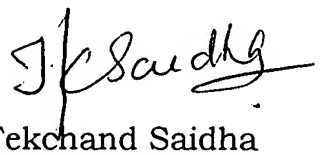
A shortened statutory period for response to this final action is set to expire THREE MONTHS from the date of this action. In the event a first response is filed within TWO MONTHS of the mailing date of this final action and the

advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event will the statutory period for response expire later than SIX MONTHS from the date of this final action.

18. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Tekchand Saidha whose telephone number is (571) 272 0940. The examiner can normally be reached on 8.30 am - 5.00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on (571) 272 0928. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



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